

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Reinhold Kerb et al.
Application No. : 10/525,360
Filed : August 22, 2003
Confirmation No. : 6836
For : POLYMORPHISMS IN THE HUMAN GENES FOR
OCT1 AND THEIR USE IN DIAGNOSTIC AND
THERAPEUTIC APPLICATIONS
Group Art Unit : 1634
Examiner : Diana B. Johannsen

New York, New York
January 14, 2009

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants make the following references of record in the above-identified patent application:¹

¹ For the Examiner's convenience, applicants have also enclosed a completed Form PTO/SB/08A/B, listing these documents.

UNITED STATES PATENTS

<u>Patent/Application No.</u>	<u>Publication Date</u>	<u>Inventor</u>
2001-0049586	12-06-2001	Roses
6,287,850	09-11-2001	Besemer et al.
5,474,796	12-12-1995	Brennan

FOREIGN PATENT DOCUMENTS

<u>Publication No.</u>	<u>Publication Date</u>
WO 94/29469	12-22-1994
WO 97/00957	01-09-1997

OTHER DOCUMENTS

Anderson, "Human Gene Therapy," *Science* 256(5058):808-813 (1992).

Arndt et al., "Interaction of cations, anions, and weak base quinine with rat renal cation transporter rOCT2 compared with rOCT1," *Am J Physiol Renal Physiol.*, 281(3):F454-F468 (2001).

Bader, "The relative power of SNPs and haplotype as genetic markers for association tests. *Pharmacogenomics*," 2(1):11-24 (2001).

Berry et al., "A Prototype Computer System for de novo Protein Design," *Biochem Soc Trans.*, 22(4):1033-1036 (1994).

Bertz et al., "Use of in vitro and in vivo data to estimate the likelihood of metabolic pharmacokinetic interactions. *Clin Pharmacokinet.*" 32(3):210-258 (1997).

Briz et al., "Carriers involved in targeting the cytostatic bile acid-cisplatin derivatives cis-diammine-chloro-cholylglycinate-platinum(II) and cis-diammine-bisursodeoxycholate-platinum(II) toward liver cells," *Mol Pharmacol.*, 61(4):853-860 (2002).

Brown et al., "Hepatotoxicity of antimicrobial agents," *Semin Liver Dis.* 22(2):157-167 (2002).

Caplin et al., "LightCycler™ Hybridization Probes," *Biochemica*, 1:5-8 (1999).

Chen et al., "Maintenance of Serotonin in the Intestinal Mucosa and Ganglia of Mice that Lack the High-Affinity Serotonin Transporter: Abnormal Intestinal Motility and the Expression of Cation Transporters," *J. Neurosci.* 21(16):6348-6361 (2001).

Cheung et al., "Making and reading microarrays," *Nat Genet.*, 21(1):15-19 (1999)

Chitturi et al., "Hepatotoxicity of commonly used drugs: nonsteroidal anti-inflammatory drugs, antihypertensives, antidiabetic agents, anticonvulsants, lipid-lowering agents, psychotropic drugs," *Semin Liver Dis.*, 22(2):169-183 (2002).

Domer et al., "The Synthesis of Peptidomimetic Combinatorial Libraries Through Successive Amide Alkylations," *Bioorg. Med Chem.*, 4(5):709-715 (1996).

Engel et al., "Prediction of CYP2D6-mediated polymorphic drug metabolism (sparteine type) based on in vitro investigations," *Journal of Chromatography B*, 29:678(1):93-103 (1996).

Fassina et al., "Identification of interactive sites of proteins and protein receptors by computer-assisted searches for complementary peptide sequences," *Immunomethods*, 5(2):114-120 (1994).

Galfre et al., "Preparation of monoclonal antibodies: strategies and procedures," *Meth. Enzymol.*, 73:3-46 (1981).

Giordano, "Intracoronary Gene Transfer of Fibroblast Growth Factor-5 Increases Blood Flow and Contractile Function in an Ischemic Region of the Heart," *Nat. Med.*, 2(5):534-539 (1996).

Gorboulev et al., "Cloning and characterization of two human polyspecific organic cation transporters," *DNA Cell Biol.*, 16(7):871-881 (1997).

Hayer-Zillgen et al., "Expression and pharmacological profile of the human organic cation transporters hOCT1, hOCT2 and hOCT3," *Br J Pharmacol.*, 136(6):829-836 (2002).

Hoffman et al., "Rapid protein structure classification using one-dimensional structure profiles on the BioSCAN parallel computer," *CABIOS*, 11(6): 675-679 (1995).

Isner et al., "Clinical Evidence of Angiogenesis After Arterial Gene Transfer of phVEGF₁₆₅ in Patient with Ischaemic Limb," *The Lancet*, 348(9024):370-374 (1996).

Jansen et al., "Bile formation and cholestasis," *Ned Tijdschr Geneesk.*, 144(50):2384-2391 (2000).

Judson et al., "Notes from the SNP vs. haplotype front," *Pharmacogenomics*. 2(1):7-10 (2001).

Judson et al., "The predictive power of haplotypes in clinical response" *Pharmacogenomics*, 1(1):15-26, (2000).

- Kimura et al., "Human Organic Anion Transporters and Human Organic Cation Transporters Mediate Renal Transport of Prostaglandins," *J. Pharmacol. Exp. Ther.*, 301(1):293-298 (2002).
- Klein et al., "An inventory of the human ABC proteins," *Biochimica et Biophysica Acta. Biomembranes*, 1461(2):237-262 (1999).
- Koeler et al., "Continuous cultures of fused cells secreting antibody of predefined specificity," *Nature*, 256:495-497 (1975).
- Koepsell et al., "Molecular pharmacology of organic cation transporters in kidney," *J Membr Biol.*, 167(2):103-17 (1999).
- Le Mouellic et al., "Targeted replacement of the homeobox gene Hox-3.1 by the Escherichia coli lacZ in mouse chimeric embryos," *Proc. Natl. Acad. Sci. USA*, 87:4712-4716 (1990).
- Lewis, "Drug-induced liver disease," *Med Clin North Am.*, 84(5):1275-1311 (2000).
- Lofius et al., "Genome duplications and other features in 12 Mb of DNA sequence from human chromosome 16p and 16q," *Genomics*, 60(3):295-308 (1999).
- Malmborg et al., "BIAcore as a tool in antibody engineering," *Journal of Immunological Methods*, 183(1):7-13 (1995).
- Marshall, "Getting the right drug into the right patient," *Nature Biotechnology*, 15: 1249 - 1252 (1997).
- Marshall, "Laying the foundations for personalized medicines," *Nature Biotechnology*, 15:954-957 (1997).
- Meyer et al., "Molecular mechanisms of genetic polymorphisms of drug metabolism," *Annu Rev Pharmacol Toxicol.*, 37:269-396 (1997).
- Meyer, "Overview of Enzymes of Drug Metabolism," *J. Pharmacokinetics Biopharm.*, 24(5):449-459 (1996).
- Meyer-Wentrup et al., "Membrane localization of the electrogenic cation transporter rOCT1 in rat liver," *Biochem Biophys Res Commun.*, 248(3):673-678. (1998).
- Mohi-ud-din, et al., "Drug- and chemical-induced cholestasis," *Clin Liver Dis.*, 95-132 (2004).
- Monge et al., "Computer Modeling of Protein Folding: Conformational and Energetic Analysis of Reduced and Detailed Protein Models," *Journal of Molecular Biology*, 247(5): 995-1012 (1995).
- Muhlhauser et al., "VEGF₁₆₅ Expressed by a Replication-Deficient Recombinant Adenovirus Vector Induces Angiogenesis In Vivo," *Circ. Res.*, 77(6):1077-1086 (1995).
- Oefner, "Allelic discrimination by denaturing high-performance liquid chromatography,"

J Chromatogr B, 739(2):345-355 (2000).

Olszewski et al., "Folding simulations and computer redesign of protein A three-helix bundle motifs," *Proteins*, 25(3):286-299 (1996).

Ostresh et al., "Generation and Use of Nonsupport-Bound Peptide and Peptidomimetic Combinatorial Libraries," *Methods Enzymol.*, 267:220-234 (1996).

Ozawa, "Strategic Proposals for Avoiding Toxic Interactions with Drugs for Clinical Use During Development and After Marketing of a New Drug--Proposals for Designing Non-Clinical Studies--Is the Non-Clinical Study Useful?," *J. Toxicol. Sci.*, 21(5):323-329 (1996).

Pabo et al., "Computer-Aided Model-Building Strategies for Protein Design," *Biochemistry*, 25(20):5987-5991 (1986).

Pearson et al., "Improved tools for biological sequence comparison," *Proc Natl Acad Sci U S A*, 85(8):2444-2448 (1998).

Perdu et al., "Identification of novel polymorphisms in the pM5 and MRPI (ABCC1) genes at locus 16p13.1 and exclusion of both genes as responsible for pseudoxanthoma elasticum," *Human Mutation*, 17(1):74-75 (2001).

Priebe et al., "Doxorubicin- and daunorubicin-glutathione conjugates, but not unconjugated drugs, competitively inhibit leukotriene C4 transport mediated by MRP/GS-X pump," *Biochemical and Biophysical Research Communications*, 247(3):859-63 (1998).

Renouf et al. "Molecular modelling of glycoproteins by homology with non-glycosylated protein domains, computer simulated glycosylation and molecular dynamics," *Adv Exp Med Biol.*, 376:37-45 (1995).

Rose et al., "Three-Dimensional Structures of HIV-1 and SIV Protease Product Complexes," *Biochemistry*, 35(39):12933-12944 (1996)

Rutenber et al., "A New Class of HIV-1 Protease Inhibitor: the Crystallographic Structure, Inhibition and Chemical Synthesis of an Aminimide Peptide Isostere," *Bioorg. & Med. Chem.*, 4(9):1545-1558 (1996)

Schaper et al., "Molecular Mechanisms of Coronary Collateral Vessel Growth," *Circ. Res.*, 79(5):911-919 (1996).

Schaper et al., "Therapeutic Targets in Cardiovascular Disorders," *Curr. Opin. Biotechnol.*, 7(6):635-640 (1996)

Schier et al., "Efficient in vitro affinity maturation of phage antibodies using BIAcore guided selections," *Hum. Antibod. Hybridomas*, 7:97-105 (1996).

Shi, "Enabling large-scale pharmacogenetic studies by high-throughput mutation

detection and genotyping technologies," *Clin Chem.*, 47(2):164-172 (2001).

Siitari, "Nucleic Acids Diagnostics Market," Technology Review 125/2002, National Technology Agency, Helsinki (2002).

Stieger et al., "Drug- and estrogen-induced cholestasis through inhibition of the hepatocellular bile salt export pump (Bsep) of rat liver," *Gastroenterology*, 118(2):422-430 (2000).

Underhill et al. "Detection of Numerous Y Chromosome Biallelic Polymorphisms by Denaturing High-Performance Liquid Chromatography," *Genome Res.*, 7: 996-1005 (1997).

van Montfoort et al., "Comparison of "type I" and "type II" organic cation transport by organic cation transporters and organic anion-transporting polypeptides," *J Pharmacol Exp Ther.*, 298(1):110-5 (2001).

Wang et al., "Second-Generation Adenovirus Vectors," *Nature Medicine*, 2(6):714-716 (1996).

Watson et al., "Technology for microarray analysis of gene expression," *Current Opinion in Biotechnology*, 9(6):609-614 (1998).

Wessler et al., "Release of non-neuronal acetylcholine from the isolated human placenta is mediated by organic cation transporters," *Br J Pharmacol.*, 134(5):951-956 (2001).

West et al., "Interpatient Variability: Genetic Predisposition and Other Genetics Factors," *J. Clin. Pharmacol.*, 37(7):635-648 (1997).

Williams et al., "Introduction of Foreign Genes into Tissues of Living Mice by DNA-Coated Microprojectiles," *Proc. Natl. Acad. Sci. USA*, 88(7):2726-2730 (1991).

Wodak, "Computer-Aided Design in Protein Engineering," *Annals N. Y. Acad. Sci.*, 501:1-13 (1987).

Zhang et al., "Interactions of HIV Protease Inhibitors with a Human Organic Cation Transporter in a Mammalian Expression System," *Drug Metab. Dispos.*, 28(3): 329-334 (2000).

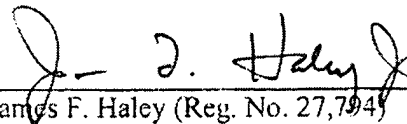
Zhang et al., "Cloning and functional expression of a human liver organic cation transporter," *Molecular Pharmacology*, 51(6):913-921 (1997).

REMARKS

Applicants further request that the cited documents be (1) fully considered by the Examiner during the course of examination of this application, and (2) printed on any patent issuing from this application. Additionally, applicants request that a copy of Form PTO/SB/08A/B, as considered and initialed by the Examiner, be returned with the next communication.

This Statement is submitted more than three months from the application filing date and after the mailing date of the first Office Action on the merits, but before the mailing date of either a final action under 37 C.F.R. § 1.113, or a notice of allowance under 37 C.F.R. § 1.311. In accordance with 37 C.F.R. § 1.97, this Statement is accompanied by the fee as set forth in 37 C.F.R. § 1.17(p). The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 06-1075, Order No. 106153-0011-101.

Respectfully submitted,



James F. Haley (Reg. No. 27,794)
Attorney for Applicants

ROPES & GRAY LLP
Customer No. 1473
1211 Avenue of the Americas
New York, New York 10036-8704
Tel.: (212) 596-9000
Fax: (212) 596-9090